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# The Council For Tobacco Research–U.S.A., Inc.

110 EAST 59TH STREET
NEW YORK, N. Y. 10022
(212) 421-8885

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Application for Research Grant
(Use extra pages as needed)

Date: June 16th, 1975

1. Principal Investigator (give title and degrees):

- Lauweryns, Joseph-M., M.D., Ph.D., Professor Ordinarius in Microscopic Anatomy and Pathology ; Chairman, Principal Investigator.

2. Institution & address:

Experimental Laboratory of Pulmonary Histopathology, Department of Pathology, University of Leuven, 12, Minderbroedersstraat, B - 3000 LEUVEN - BELGIUM.

3. Department(s) where research will be done or collaboration provided:

Experimental Laboratory of Pulmonary Histopathology, Department of Pathology, University of Leuven, 12, Minderbroedersstraat, B - 3000 LEUVEN - BELGIUM.

4. Short title of study:

The Neuro-epithelial Bodies : their role and structure as intrapulmonary neuro(chemo) receptors in normal and various physiological, pharmacological and pathological conditions.

5. Proposed starting date: January 1, 1976 (first year)

6. Estimated time to complete: From January 1, 1976 till December 31st, 1978.

7. Brief description of specific research aims:

We recently identified throughout the intrapulmonary airways of the human and mammalian lung intramucosal corpuscles or so-called Neuro-epithelial Bodies (NEB's), whose general characteristics have been described in the hereby included pertinent publications. From these earlier observations and preliminary experiments on the effect of hypoxia on these NEB's, we have suggested that the NEB's may provide an intrapulmonary, hypoxia sensitive neuro(chemo)receptor system modulated by the central nervous system in addition to the well-known central and peripheral chemoreceptors. They contain and secrete serotonin and probably also related amines and peptides, which could influence the pulmonary vasoconstrictor response. They could however have various other possible functions, modulating not only pulmonary vasomotion, but also bronchial and bronchiolar mucosal secretion or smooth muscle tone.

During the three-years of this research proposal (1976-1978) we intend to study the pulmonary NEB's along three major lines of investigation : - (1) a further and thorough investigation of their normal morphology, and especially their relationship to the Kultschitzky-like cells and the APUD-series, - (2) an experimental study of their structural reactions under various physiological (hypoxia, hyperoxia, hypoxemia, cross-circulation) and pharmacological (L-DOPA, 5-HTP, nicotine) conditions, - and (3) a light optical study of their incidence and size in lung diseases, mainly associated with hypoxia.

Various techniques which complement each other and are all familiar to us, will be applied : - light optics, histochemistry, morphometry, fluorescence microscopy, microspectrography, transmission electron microscopy and scanning electron microscopy.

Though the lines of investigation are distinct, the study object is identical and the results interrelated. These studies will necessarily end in important and original basic and applied results as regards the structure and functions of the normal and diseased lung. It is obvious that these studies are of immediate and relevant importance in biological tobacco research.

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Source: https://www.industrydocuments.ucsf.edu/docs/xpdm0000

8. Brief statement of working hypothesis:

Having identified the occurrence of NEB's in the human and mammalian lung, it is obviously indicated to apply furthermore the tools of a combined and multidisciplinary investigation to unravel their fine structure and function. This study will moreover benefit of the experience of the same team of investigators who work closely together since several years and who have their personal skill as regards the various techniques to be used.
The NEB's appear as a new area of promising future research and discovery in various basic fields of pulmonary function and structure (e.g. hypoxic pulmonary vasoconstriction).

9. Details of experimental design and procedures (append extra pages as necessary)

See separate pages - Addendum 1

Please note moreover :

During this three-year (1976-1978) research program - outlined in "addendum 1 (details of experimental design and procedures) - we have proposed to study the NEB's along three major lines of investigation, i.e. :

- (1) Further studies on the normal morphology of the NEB's
- (2) An experimental study of the structural reactions of the NEB's under various physiological (hypoxia, hyperoxia, hypoxemia, cross-circulation) and pharmacological (L-DOPA, 5-HTP, nicotine) conditions, and
- (3) A light optical study of the incidence and size of the NEB's in pathological conditions in the human lung.

Though we will start the investigation of the three items at the same time, we will mainly concentrate our efforts during this first year (1976) on item # 2.

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10. Space and facilities available (when elsewhere than item 2 indicates, state location):

- All physical facilities are available at our laboratory (as mentioned under item 2), and we will have facilities for scanning electron microscopy either at the university of Ghent or Leuven.
- Separate list of these physical facilities - see addendum 2

11. Additional facilities required:

None

i.e. - Lauweryns, Joseph-M., M.D., Ph.D., principal investigator.
- Cokelaere Marnix, Lic. Biol. Sc., full-time research assistant, doctorandus, Co-investigator.
- Liebens Marc, Lic. Biol. Sc., full-time research assistant, Co-investigator.

12. Biographical sketches of investigator(s) and other professional personnel (append):

See separate pages - Addendum 3

13. Publications: (five most recent and pertinent of investigator(s); append list, and provide reprints if available).

Publications on the NEB's - see Addendum 4
Progress Report of Grant No. 741B, No. 741C - see Addendum 5

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14. First year budget:

A. Salaries (give names or state "to be recruited")

| Professional (give % time of investigator(s) even if no salary requested) | % time | Amount |
|---|---|---|
| - Lauweryns Joseph | 60 % | none |
| - Cokelaere Marnix | 90 % | none |
| - Liebens Marc | 90 % | none |
| Technical | | |
| - Two laboratory technicians (Kris ARMEE ; Stefaan ONS) | 100 % | 16,196 |

Sub-Total for A 16,196

B. Consumable supplies (by major categories)

| | |
|---|---|
| Animals | 3,024 |
| supplies | 13,200 |

Sub-Total for B 16,224

C. Other expenses (itemize)

Sub-Total for C none

Running Total of A + B + C 32,420

D. Permanent equipment (itemize)

Sub-Total for D none

E. Indirect costs (15% of A+B+C) E none

Total request 32,420

15. Estimated future requirements:

| | Salaries | Consumable Suppl. | Other Expenses | Permanent Equip. | Indirect Costs | Total |
|---|---|---|---|---|---|---|
| Year 2 | 17.816 | 17.846 | | | | 35.662 |
| Year 3 | 19.598 | 19.631 | | | | 39.229 |

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16. Other sources of financial support:
List financial support from all sources, including own institution, for this and related research projects.

CURRENTLY ACTIVE

| Title of Project | Source (give grant numbers) | Amount | Inclusive Dates |
|---|---|---|---|
| Morphological studies of the lung. | University of Leuven | | |
| | J.M. Lauweryns, Professor, salary | $ 24,000 | yearly |
| | M. Cokelaere, assistant salary | $ 12,000 | yearly |
| | M. Liebens, assistant salary | $ 12,000 | yearly |
| | Salary of 2 technicians | $ 17,400 | yearly |
| | Supplies and animals | $ 7,600 | yearly |

PENDING OR PLANNED

| Title of Project | Source (give grant numbers) | Amount | Inclusive Dates |
|---|---|---|---|
| | | | |

It is understood that the investigator and institutional officers in applying for a grant have read and accept the Council's "Statement of Policy Containing Conditions and Terms Under Which Project Grants Are Made."

Principal investigator

Typed Name Joseph M. LAUWERYNS

Signature J. Lauweryns Date June 16th, 75

Telephone 016 (Area Code) 22.89.81 (Number) (Extension)

Checks payable to

Prof. P. DE SOMER, Rector of the University

Mailing address for checks

Dr. P. DE SOMER, Rector, Catholic University of Leuven
B - 3000 LEUVEN - BELGIUM

Responsible officer of institution

Typed Name Pieter DE SOMER

Title Rector

Signature [illegible] Date June 20th, 75

Telephone 016 (Area Code) 22.04.31 (Number) 131 or 116 (Extension)

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